

MAY 29 2002

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<110> Daniel Cchen  
Ilya Chumakov

<120> Treatment of CNS Disorders Using D-Amino Acid Oxidase and D-Aspartate  
Oxidase Antagonists

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Ile Gly Leu Ser Thr Ala Leu Cys Ile His Glu Arg Tyr His Ser Val 25  
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Tnr Thr Thr Asp Val Ala Ala Gly Leu Trp Glu Pro Tyr Leu Ser Asp	45	50	55	
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Leu Ile Ser Gly Tyr Asn Leu Phe His Glu Ala Ile Pro Asp Pro Ser				
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Trp Lys Asp Thr Val Leu Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu				
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Arg Gly Val Lys Phe Phe Gln Arg Lys Val Glu Ser Phe Glu Glu Val				
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Ala Arg Glu Gly Ala Asp Val Ile Val Asn Cys Thr Gly Val Trp Ala				
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Thr Val Thr Leu Leu Gly Gly Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu				
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Glu Pro Thr Lys Thr Lys Asn Ala Arg Ile Ile Gly Glu Arg Thr Gly Phe				
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Arg Pro Val Arg Pro Gln Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr				
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Gly Pro Ser Asn Thr Glu Val Ile His Asn Tyr Gly His Gly Gly Tyr				
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Gly Leu Thr Ile His Trp Gly Cys Ala Leu Glu Ala Leu Lys Leu Phe				
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Cys Ile His Glu Arg Tyr His Ser Val Leu Gln Pro Leu Asp Ile Lys
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Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly Ile Phe Gln
165 170 175
ttg gga aac tgg agt gaa cta aac aat atc cag gac cac aac acc att 692
Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His Asn Thr Ile
180 185 190
tgg gaa ggc tgc tgc aga ctg gag ccc aca ctg aag aat gca aga att 740
Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn Ala Arg Ile
195 200 205
att ggt gaa cga act ggc ttc cgg cca gta cgc ccc cag att cgg cta 788
Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln Ile Arg Leu
210 215 220 225
gaa aga gaa cag ctt cgc att gga cct tca aac aca gag gtc atc cac 836
Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu Val Ile His

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	230	235	240	
aac tat ggc cat gga ggc tac ggg ctc acc atc cac tgg gga tgt gcc				884
Asn Tyr Gly His Gly Gly Tyr Gly Leu Thr Ile His Trp Gly Cys Ala				
	245	250	255	
ctg gag gca gcc aag ctc ttt ggg aga atc ctg gaa gaa aag aaa ttg				942
Leu Glu Ala Ala Lys Leu Phe Gly Arg Ile Leu Glu Glu Lys Lys Leu				
	260	265	270	
tcc aga atg cca cca tcc cac ctc tgaagatccc agtgaatgct gccccccccc				986
Ser Arg Met Pro Pro Ser His Leu				
	275	280		
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tggaagaaggg ttcagcccaa ccagggggccc ctctcctcac tgaattcccc ctactctctc				1166
tggtctctggc attataaaga acagctgagg ctgtcattcc atgagtcttc agtagaaagg				1226
acagctcaga aaatcaaga ggcacaactgc ccagagccac agaaaaagga ggataattga				1286
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 Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Thr Asp Val Ala  
 35 40 45  
 Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu  
 50 55 60  
 Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His  
 65 70 75 80  
 Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn  
 85 90 95  
 Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu  
 100 105 110  
 Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met Phe Pro Asp Tyr  
 115 120 125  
 Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu Glu Gly Lys Asn Tyr  
 130 135 140  
 Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly Val Lys Phe Phe  
 145 150 155 160  
 Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp  
 165 170 175  
 Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp  
 180 185 190  
 Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro  
 195 200 205  
 Trp Met Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr  
 210 215 220  
 Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly  
 225 230 235 240  
 Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His  
 245 250 255  
 Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn  
 260 265 270  
 Ala Arg Ile Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln  
 275 280 285

Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu  
 290 295 300  
 Val Ile His Asn Tyr Gly His Gly Gly Tyr Gly Leu Thr Ile His Trp  
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 Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe Gly Arg Ile Leu Glu Glu  
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 Lys Lys Leu Ser Arg Met Pro Pro Ser His Leu  
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 Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Thr Asp Val Ala  
 35 40 45  
 Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu  
 50 55 60  
 Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His  
 65 70 75 80  
 Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn  
 85 90 95  
 Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu  
 100 105 110  
 Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met Phe Pro Asp Tyr  
 115 120 125  
 Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu Glu Gly Lys Asn Tyr  
 130 135 140  
 Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly Val Lys Phe Phe  
 145 150 155 160  
 Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp  
 165 170 175  
 Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp  
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 Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Asp Pro Asp Ser  
 195 200 205  
 Tyr Ser Trp Arg His Leu Pro Val Gly Lys Leu Glu  
 210 215 220

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 Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Thr Asp Val Ala  
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 Leu Cys Ile His Glu Arg Tyr His Ser Val Leu Gln Pro Leu Asp Ile  
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 Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Thr Asp Val Ala  
 35 40 45  
 Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu  
 50 55 60  
 Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His  
 65 70 75 80  
 Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn  
 85 90 95  
 Leu Phe His Glu Ala Ile Pro Val Ala Arg Glu Gly Ala Asp Val Ile  
 100 105 110  
 Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp Pro Leu  
 115 120 125  
 Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro Trp Met  
 130 135 140  
 Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr Asn Ser  
 145 150 155 160  
 Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly Ile Phe  
 165 170 175  
 Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His Asn Thr  
 180 185 190  
 Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn Ala Arg  
 195 200 205  
 Ile Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln Ile Arg  
 210 215 220  
 Leu Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu Val Ile  
 225 230 235 240  
 His Asn Tyr Gly His Gly Gly Tyr Gly Leu Thr Ile His Trp Gly Cys  
 245 250 255  
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 260 265 270  
 Leu Ser Arg Met Pro Pro Ser His Leu  
 275 280

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 <223> 99-16105-152 : polymorphic base A or G

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attaaaaatag cttgtaggat tactcatttt cttttttctt ctttttaaat ataaagcaat 180
gtcaccaactt ttttccctgt attatatttc tctcaataa ttgatatgct acattaaagg 240
aacacaaaaat ggtottaatt atgcaataat gatcaaggca aagagtgttt cctgggaact 300
aatgggtgcc tgagaggagg tgatggcttg aggtccagct ggttattaag ccgcaggaaa 360
tgctgcaggc caagatttgt attattctc tgatagaaa atgaaccaa aaaaaggcaa 420
aatgggtttt tctccactaa tgggtaaaaat gaactc 456

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<222> 203..227
<223> 99-5919-215.probe

<220>
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<222> 196..214
<223> 99-5919-215.mis

<220>
<221> primer_bind
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<223> 99-5919-215.mis complement

<220>
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<222> 11..29

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4223> 99-5919.pu

<120>

<21> primer\_bind

<22> 445..465

<23> 99-5919.rp complement

<400> 13

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actacacaaa	atcacctttt	cctgtataca	tttttaggat	gtcagacttt	attctaatga	180
tttctcttag	ttgcccccca	aaattgtatt	ctacrgtggtg	attttaaagc	tgaattttca	240
agtctatatt	tcatatctat	attttcacaa	gcttttcttc	tatgaatggt	attgtcagct	300
gtcgggtgtg	gagatggtac	ttgatactac	attctttcca	agctgttgcc	tgaatcggtt	360
tacacacaag	tcattantag	gcgtaaaact	gttgcctctg	aaaattgagc	agcactgatt	420
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<210> 13

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<222> 509..742

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<222> 718..723

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<222> 21

<223> 8-135-112 : polymorphic base C or T

<220>

<221> allele

<222> 75

<223> 8-135-166 : polymorphic base A or C

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<221> allele

<222> 135

<223> 99-16038-118 : polymorphic base A or G

<220>

<221> allele

<222> 194

<223> 8-137-152 : polymorphic base G or T

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 <222> 194  
 <223> Xaa=Glu or Stop  
  
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 <223> Xaa=Gly or Arg  
  
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 lys Leu Met Gly Ala Asp Xaa Leu Gln Leu Phe Arg Ser Arg Tyr Thr  
 5 10 15  
 ttg ggt aaa atc tac ttc ata ggt ttt caa arg aga att ctt ctg agc 151  
 leu Gly Lys Ile Tyr Phe Ile Gly Phe Gln Xaa Ser Ile Leu Leu Ser  
 20 25 30 35  
 aaa tct gaa aac tct cta aac tct att gca aag gag aca gaa kaa gga 159  
 lys Ser Glu Asn Ser Leu Asn Ser Ile Ala Lys Glu Thr Glu Xaa Gly  
 40 45 50  
 aha gag acg gta aca agg aaa gaa rga tgg aag aga agg cat gag gac 247  
 Arg Glu Thr Val Thr Arg Lys Glu Xaa Trp Lys Arg Arg His Glu Asp  
 55 60 65  
 gac tat ttg gaa atg gca cag agg cat tta cag aga tca tta tgt cct 295  
 Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser Leu Cys Pro  
 70 75 80  
 tgg gtc tct tac ctt cct cag ccc tat gca gag ctt gaa gaa gta agc 342  
 Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu Glu Val Ser  
 85 90 95  
 aac cat gtt gga aaa gtc ttc atg gca aga aac tat gag ttc ctt gmc 391  
 Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu Phe Leu Xaa  
 100 105 110 115  
 tat gag gcc tct aar gac cgc agg cag cct cta gaa cga atg tgg acc 439  
 Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg Met Trp Thr  
 120 125 130  
 tgc aac tac aac cag caa aaa gac cag tca tgc aac cac aag gaa ata 487  
 Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His Lys Glu Ile  
 135 140 145  
 act tct acc aaa gct gaa tgagtttgga agcagattct tccagccaa 535  
 Thr Ser Thr Lys Ala Glu  
 150  
 tctttctgat gacaatgtag tctggccaac atcttcaactg gamtctgaoc gactctgtgt 595  
 ctgggaccca gctgataaca cgtggtgatg ggattgtatt tgcaayctctc tggtcagtaa 655  
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 <212> PRT  
 <213> Homo sapiens

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<223> basic protease cleavage site

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<120>
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<120> 132..142

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<120> 124..153

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Arg Tyr Thr Leu Gly Lys Ile Tyr Phe Ile Gly Phe Gln Xaa Ser Ile
20      25      30
Leu Leu Ser Lys Ser Glu Asn Ser Leu Asn Ser Ile Ala Lys Glu Thr
35      40      45
Glu Xaa Gly Arg Glu Thr Val Thr Arg Lys Glu Xaa Trp Lys Arg Arg
50      55      60
His Glu Asp Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser
65      70      75      80
Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu
85      90      95
Gln Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu
100     105     110
Phe Leu Xaa Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg
115     120     125
Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His
130     135     140
Lys Glu Ile Thr Ser Thr Lys Ala Glu
145     150

<210> 15

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<211> 476

<212> DNA

<213> Homo sapiens

<400> 15

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1      5      10      15
tra tgt cct tgg gtc tct tac ctt cct cag ccc tat gca gag ctt gaa      96
Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu
20     25     30
gaa gta agc agc cat gtt gga aaa gtc ttc atg gca aga aac tat gag      144
Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu
35     40     45
ttc ctt gcc tat gag gcc tct aag gac cgc agg cag cct cta gaa cga      192
Phe Leu Ala Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg
50     55     60
arg tgg acc tgc aac tac aac cag caa aaa gac cag tca tgc aac cag      240
Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His
65     70     75     80
aag gaa ata act tct acc aaa gct gaa tgagtcttgga agcagattct      287
Lys Glu Ile Thr Ser Thr Lys Ala Glu
85
tccagagcaaa tctcttgat gacaatgtag tctggccaac atcttccactg gactctgacg      347
gactctgtgt ctgggaccca gctgataaca cgtgggtgatg ggattgtatt tgcacactctc      407
tggtcagtaaa gtgataaaat gccatttcta tgcacccacc tggcctgtgt gactgggaga      467
atctctcttc      476
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<210> 16

<211> 89

<212> FRT

<213> Homo sapiens

<400> 16

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Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu
20     25     30
Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu
35     40     45
Phe Leu Ala Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg
50     55     60
Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His
65     70     75     80
Lys Glu Ile Thr Ser Thr Lys Ala Glu
85
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<210> 17

<211> 1633

<212> DNA

<213> Homo sapiens

<400> 17

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tgggtgcacg tggaaaggcg acagagggct ggaacaaga cgtccagaa tcaggagctt      120
ccctcagga aatagatccc tctgtccccc cactgcagtt gtctggtctc tccagcagtt      180
tggtaacttc ggcctgtgca atg cgt gtg gtg gtg att gga gca gga gtc atc      233
Met Arg Val Val Val Ile Gly Ala Gly Val Ile
1      5      10
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ggg ctg tcc acc gcc ctg tgc atc cat gag cgc tac cac tca gtc ctg 281  
 Gly Leu Ser Thr Ala Leu Cys Ile His Glu Arg Tyr His Ser Val Leu  
 15 20 25  
 cag cca ctg cac ata aag ggc tac ggc gac cgc ttc acc cca ctg acc 329  
 Gln Pro Leu His Ile Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr  
 30 35 40  
 acc acc gac gtc ggt ggc gac ctg tgg cag ccc ttc ctt tct gac ccc 377  
 Thr Thr Asp Val Ala Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro  
 45 50 55  
 aac aac cca cag gag ggc gac tgg agc caa cag acc ttt gac tat ctg 425  
 Asn Asn Pro Gln Glu Ala Asp Trp Ser Gln Thr Phe Asp Tyr Leu  
 60 65 70 75  
 ctg agc cat gtc cat tct ccc aac gct gaa aac ctg ggc ctg ttc cta 473  
 Leu Ser His Val His Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu  
 80 85 90  
 atc tgg ggc tac aac ctg ttc cat gaa gcc att cgg gac cct tcc tgg 521  
 Ile Ser Gly Tyr Asn Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp  
 95 100 105  
 aag gac aca gtt ctg gga ttt cgg aag ctg acc ccc aga gac ctg gat 569  
 Thr Asp Thr Val Leu Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp  
 110 115 120  
 atg ttc cca gat tac ggc tat ggc tgg ttc cac aca agc cta att ctg 617  
 Met Phe Pro Asp Tyr Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu  
 125 130 135  
 gag gga aag aac tat cta cag tgg ctg act gaa agg tta act gag agg 665  
 Glu Gly Lys Asn Tyr Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg  
 140 145 150 155  
 gga gtc aag ttc ttc cag cgg aaa gtc gag tct ttt gag gag gtc gca 713  
 Gly Val Lys Phe Phe Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala  
 160 165 170  
 aga gaa ggc gca gac gtc att gtc aac tgc act ggg gta tgg gct ggg 761  
 Arg Glu Gly Ala Asp Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly  
 175 180 185  
 ggc cta caa cga gac ccc ctg ctg cag cca ggc cgg ggg cag atc atg 809  
 Ala Leu Gln Arg Asp Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met  
 190 195 200  
 aag gtc gac gcc cct tgg atg aag cac ttc att ctg acc cat gac cca 857  
 Lys Val Asp Ala Pro Trp Met Lys His Phe Ile Leu Thr His Asp Pro  
 205 210 215  
 gag aga ggc atc tac aat tcc cgg tac atc atc cca ggg acc cag aca 905  
 Glu Arg Gly Ile Tyr Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln Thr  
 220 225 230 235  
 gtt act ctt gga ggc atc ttc cag ttg gga aac tgg agt gaa cta aac 953  
 Val Thr Leu Gly Gly Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu Asn  
 240 245 250  
 aat atc cag gac cac aac acc att tgg gaa ggc tgc tgc aga ctg gag 1001  
 Asn Ile Gln Asp His Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu Glu  
 255 260 265  
 ccc aca ctg aag aat gca aga att att ggt gaa cca act ggc ttc cgg 1049  
 Pro Thr Leu Lys Asn Ala Arg Ile Ile Gly Glu Ala Thr Gly Phe Arg  
 270 275 280  
 cca gta cgc ccc cag att cgg cta gaa aga gaa cag ctt cgc act gga 1097  
 Pro Val Arg Pro Gln Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr Gly  
 285 290 295  
 cct tca aac aca gag gtc atc cac aac tat ggc cat gga ggc tac ggg 1145  
 Pro Ser Asn Thr Glu Val Ile His Asn Tyr Gly His Gly Tyr Gly  
 300 305 310 315  
 ctg acc atc cac tgg gga tgt gcc ctg gag gca gcc aag ctg ttt ggg 1193  
 Leu Thr Ile His Trp Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe Gly

aga atc ctg gaa gaa aag aaa ttg tcc aga atg cca cca tcc cac ctc	320	325	330	1241
Arg Ile Leu Glu Glu Lys Lys Leu Ser Arg Met Pro Pro Ser His Leu				
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autcaagtg ctccttcata agccattgct tctccctcac tctcttccct aaagaagcat				1361
gggttgagag aaagccacra agtcagtgcc tggagaaggg ttcagcccaa catggggccc				1421
cctccatcac tgaatccct ctacattctc tgggtctggc attataaga acagctgagg				1481
ctgattctc atgattcttc agaagaaagg acagctcaga aagtcacaaga ggcccaactgc				1541
ccadaagcac aaaaaatgga qgataattga qgctaagtaa actgattaca agttgtacta				1601
acatattaaa ggttctgaaa agtccctgcaa aa				1633

<210> 18  
 <211> 347  
 <212> PRT  
 <213> Homo sapiens

<400> 18

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Leu	Cys	Ile	His	Glu	Arg	Tyr	His	Ser	Val	Leu	Gln	Pro	Leu	Asp	Ile
			20					25					30		
Lys	Val	Tyr	Ala	Asp	Arg	Phe	Thr	Pro	Leu	Thr	Thr	Thr	Asp	Val	Ala
		35					40						45		
Ala	Gly	Leu	Trp	Gln	Pro	Tyr	Leu	Ser	Asp	Pro	Asn	Asn	Pro	Gln	Glu
		50				55					60				
Ala	Asp	Trp	Ser	Gln	Gln	Thr	Phe	Asp	Tyr	Leu	Leu	Ser	His	Val	His
		65				70				75					80
Ser	Pro	Asn	Ala	Glu	Asn	Leu	Gly	Leu	Phe	Leu	Ile	Ser	Gly	Tyr	Asn
			85						90					95	
Leu	Phe	His	Glu	Ala	Ile	Pro	Asp	Pro	Ser	Trp	Lys	Asp	Thr	Val	Leu
			100					105					110		
Gly	Phe	Arg	Lys	Leu	Thr	Pro	Arg	Glu	Leu	Asp	Met	Phe	Pro	Asp	Tyr
		115					120					125			
Gly	Tyr	Gly	Trp	Phe	His	Thr	Ser	Leu	Ile	Leu	Glu	Gly	Lys	Asn	Tyr
		130				135					140				
Leu	Gln	Trp	Leu	Thr	Glu	Arg	Leu	Thr	Glu	Arg	Gly	Val	Lys	Phe	Phe
		145			150				155						160
Gln	Arg	Lys	Val	Glu	Ser	Phe	Glu	Glu	Val	Ala	Arg	Glu	Gly	Ala	Asp
			165					170					175		
Val	Ile	Val	Asn	Cys	Thr	Gly	Val	Trp	Ala	Gly	Ala	Leu	Gln	Arg	Asp
			180					185					190		
Pro	Leu	Leu	Gln	Pro	Gly	Arg	Gly	Gln	Ile	Met	Lys	Val	Asp	Ala	Pro
		195					200					205			
Trp	Met	Lys	His	Phe	Ile	Leu	Thr	His	Asp	Pro	Glu	Arg	Gly	Ile	Tyr
	210					215						220			
Asn	Ser	Pro	Tyr	Ile	Ile	Pro	Gly	Thr	Gln	Thr	Val	Thr	Leu	Gly	Gly
			225			230				235					240
Ile	Phe	Gln	Leu	Gly	Asn	Trp	Ser	Glu	Leu	Asn	Asn	Ile	Gln	Asp	His
			245					250					255		
Asn	Thr	Ile	Trp	Glu	Gly	Cys	Cys	Arg	Leu	Glu	Pro	Thr	Leu	Lys	Asn
			260					265					270		
Ala	Arg	Ile	Ile	Gly	Glu	Ala	Thr	Gly	Phe	Arg	Pro	Val	Arg	Pro	Gln
			275			280					285				
Ile	Arg	Leu	Glu	Arg	Glu	Gln	Leu	Arg	Thr	Gly	Pro	Ser	Asn	Thr	Glu
		290				295					300				
Val	Ile	His	Asn	Tyr	Gly	His	Gly	Gly	Tyr	Gly	Leu	Thr	Ile	His	Trp
		305				310				315					320
Gly	Cys	Ala	Leu	Glu	Ala	Ala	Lys	Leu	Phe	Gly	Arg	Ile	Leu	Glu	Glu

	325	330	335
Lys Lys Leu Ser Arg Met Pro Pro Ser His Leu			
	340	345	

<210> 19  
 <211> 1200  
 <212> DNA  
 <213> Homo sapiens

<400> 19

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Met Asp Thr Ala Arg Ile Ala Val Val Gly Ala Gly Val Val Gly Leu	
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ccc acg gct gtg tgc atc tcc aaa ctg gtg ccc cga tgc tcc gtt acc	96
Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr	
20 25 30	
atc att tca gac aag ttt act cca gat acc acc agt gat gtg gca gcc	144
Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala	
35 40 45	
gga atg ctt att cct cac act tat cca gat aca ccc att cac acg cag	192
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln	
50 55 60	
aag cag tgg ttc aga gaa acc ttt aat cac ctc ttt gca att gcc aat	240
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn	
65 70 75 80	
tct gca gaa gct gga gat gct ggt gtt cat ttg gta tca ggt tgg cag	288
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Trp Gln	
85 90 95	
ata ttt cag agc act cag act gaa gaa gtg cca ttc tgg gct gac gtg	336
Ile Phe Gln Ser Thr Pro Thr Glu Glu Val Pro Phe Trp Ala Asp Val	
100 105 110	
gtt ctg gga ttt cga aag atg act gag gct gag ctg aag aaa ttc ccc	384
Val Leu Gly Phe Arg Lys Met Thr Glu Ala Glu Leu Lys Lys Phe Pro	
115 120 125	
cag tat gtg ttt ggt cag gct ttt aca acc ctg aaa tgt gaa tgc cct	432
Gln Tyr Val Phe Gly Gln Ala Phe Thr Thr Leu Lys Cys Glu Cys Pro	
130 135 140	
gcc tac ctc cag tgg ttg gag aaa agg ata aag gga agt gga gcc tgg	480
Ala Tyr Leu Pro Trp Leu Glu Lys Arg Ile Lys Gly Ser Gly Gly Trp	
145 150 155 160	
aca ctc act cgg cga ata gaa gac ctg tgg gaa ctt cat ccc tcc ttt	528
Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu Leu His Pro Ser Phe	
165 170 175	
gac atc gtg gtc aac tgt tca ggc ctt gga agc aga cag ctt gca gga	576
Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser Arg Gln Leu Ala Gly	
180 185 190	
gac tca aag att ttc cct gta agg ggc caa gtc ctc caa gtt cag gct	624
Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val Leu Gln Val Gln Ala	
195 200 205	
ccc tgg gtg gag cat ttt atc cga gat ggc agt ggg ctg aca tat att	672
Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser Gly Leu Thr Tyr Ile	
210 215 220	
tat cct ggt aca tcc cat gta acc cta ggt gga act agg caa aaa ggg	720
Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly Thr Arg Gln Lys Gly	
225 230 235 240	
gac tgg aat ctg tcc cag gat gca gaa aat agc aga gag att ctt tcc	768
Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser Arg Glu Ile Leu Ser	
245 250 255	
cga tgc tgt gct ctg gag ccc tcc ctc cac gga gcc tgc aac atc agg	816



Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly Ala Cys Asn Ile Arg	260	265	270	
gag aag gtg ggc ttg agg ccc tac agg cca ggc gtg cga ctg cag aca				864
Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly Val Arg Leu Gln Thr	275	280	285	
gag ctc ttt ggc cga gat gga cag agg ctg cct gta gtc cac cac tat				912
Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro Val Val His His Tyr	290	295	300	
ggc cat ggc agt ggc ggc atc tca gtg cac tgg ggc act gct ctg gag				950
Gly His Gly Ser Gly Gly Ile Ser Val His Trp Gly Thr Ala Leu Glu	305	310	315	
gcc gcc agg ctg gtg agc gag tgt gtc cat gcc ctg agg acc ccc att				1008
Ala Ala Arg Leu Val Ser Glu Cys Val His Ala Leu Arg Thr Pro Ile	325	330	335	
ccc aag tca aac ctg tagatgacat aaaaatgacag caaagagact gagagactgt				1053
Pro Lys Ser Asn Leu	340			
tgatcaaaagc acagaacagg ttc aaataac ttttccactg caagaaggt taattagaca				1123
tttttttgt ttcacatta gaagtgtgt aacatgtaag ctgagacagg tagcatgctt				1183
atagtcacag ctacttg				1200
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Met Asp Thr Ala Arg Ile Ala Val Val Gly Ala Gly Val Val Gly Leu	5	10	15	
1				96
tcc acg gct gtg tgc atc tcc aaa ctg gtg ccc cga tgc tcc gtt acc				
Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr	20	25	30	
atc att tca gac aag ttt act cca gat acc acc agt gat gtg gca gcc				144
Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala	35	40	45	
gga atg ctt att cct cac act tat cca gat aca ccc att cac acg cag				192
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln	50	55	60	
aag cag tgg ttc aga gaa acc ttt aat cac ctg ttt gca att gcc aat				240
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn	65	70	75	
80				288
tct gca gaa gct gga gat gct ggt gtt cat ttg gta tca ggg ata aag				
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Ile Lys	85	90	95	
gga agt gga ggc tgg aca ctg act cgg cga ata gaa gac ctg tgg gaa				336
Gly Ser Gly Gly Trp Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu	100	105	110	
ctt cat cag tcc ttt gac atc gtg gtc aac tgt tca ggc ctt gga agc				384
Leu His Pro Ser Phe Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser	115	120	125	
aga cag ctt gca gga gat tca aag att ttc cct gta agg ggc caa gtc				432
Arg Gln Leu Ala Gly Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val	130	135	140	
ctc caa gtt cag gct ccc tgg gtg gag cat ttt atc cga gat ggc agt				480
Leu Gln Val Gln Ala Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser	145	150	155	
160				528
ggg ctg aca tat att tat cct ggt aca tcc cat gta acc cta ggt gga				
Gly Leu Thr Tyr Ile Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly				

act agg caa aaa ggg gac tgg aat ctg tcc ccc gat gca gaa aat agc	165	170	175	576
Thr Arg Gln Lys Gly Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser				
aga gag att ctt tcc cga tgc tgt gct ctg gag ccc tcc ctc cac gga	180	185	190	624
Arg Glu Ile Leu Ser Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly				
gac tgc aac atc agg gag aag gtg ggc tgg agg ccc tac agg cca ggc	195	200	205	672
Ala Cys Asn Ile Arg Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly				
gtg cga ctg cag aca gag ctg ctt ggc cga gat gga cag agg ctg cct	210	215	220	720
Val Arg Leu Gln Thr Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro				
gta gtc cac cac tat ggc cat ggg agt ggg ggc atc cca gtg cac tgg	225	230	235	768
Val Val His His Tyr Gly His Gly Ser Gly Gly Ile Ser Val His Trp				
gac act gct ctg gag gcc gcc agg ctg gtg agc gag tat gtc cat gcc	245	250	255	816
Gly Thr Ala Leu Glu Ala Ala Arg Leu Val Ser Glu Cys Val His Ala				
ctc agg acc ccc att ccc aag tca aac ctg tagatgacat aaaatgacag	260	265	270	866
Leu Arg Thr Pro Ile Pro Lys Ser Asn Leu				
caaaagagact gagagactgt tgatcaaacg acagaacagg ttcaataaac ttttccactg	275	280		926
catgaaagt taattagaca tttctttgtt ttcaacatta gaagcggtgt aacatgtaag				986
ctgagcagg tagcatgct atagtccag ctacttg				1023

<210> 21  
 <211> 341  
 <212> PRT  
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Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr	
20 25 30	
Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala	
35 40 45	
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln	
50 55 60	
Lys Gln Trp Phe Arg Gly Thr Phe Asn His Leu Phe Ala Ile Ala Asn	
65 70 75 80	
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Trp Gln	
85 90 95	
Ile Phe Gln Ser Thr Pro Thr Glu Glu Val Pro Phe Trp Ala Asp Val	
100 105 110	
Val Leu Gly Phe Arg Lys Met Thr Glu Ala Glu Leu Lys Lys Phe Pro	
115 120 125	
Gln Tyr Val Phe Gly Gln Ala Phe Thr Thr Leu Lys Cys Glu Cys Pro	
130 135 140	
Ala Tyr Leu Pro Trp Leu Glu Lys Arg Ile Lys Gly Ser Gly Gly Trp	
145 150 155 160	
Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu Leu His Pro Ser Phe	
165 170 175	
Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser Arg Gln Leu Ala Gly	
180 185 190	
Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val Leu Gln Val Gln Ala	
195 200 205	
Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser Gly Leu Thr Tyr Ile	

210                      315                      220  
 Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly Thr Arg Gln Lys Gly  
 225                      230                      235                      240  
 Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser Arg Glu Ile Leu Ser  
                     245                      250                      255  
 Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly Ala Cys Asn Ile Arg  
                     260                      265                      270  
 Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly Val Arg Leu Gln Thr  
                     275                      280                      285  
 Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro Val Val His His Tyr  
                     290                      295                      300  
 Gly His Gly Ser Gly Gly Ile Ser Val His Trp Gly Thr Ala Leu Glu  
 305                      310                      315                      320  
 Ala Ala Arg Leu Val Ser Glu Cys Val His Ala Leu Arg Thr Pro Ile  
                     325                      330                      335  
 Pro Lys Ser Asn Leu  
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<310> 22  
 <311> 282  
 <312> PRT  
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<400> 22  
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                     20                      25                      30  
 Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala  
 35                      40                      45  
 Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln  
 50                      55                      60  
 Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn  
 65                      70                      75                      80  
 Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Ile Lys  
                     85                      90                      95  
 Gly Ser Gly Gly Trp Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu  
                     100                      105                      110  
 Leu His Pro Ser Phe Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser  
                     115                      120                      125  
 Arg Gln Leu Ala Gly Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val  
 130                      135                      140  
 Leu Gln Val Gln Ala Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser  
 145                      150                      155                      160  
 Gly Leu Thr Tyr Ile Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly  
                     165                      170                      175  
 Thr Arg Gln Lys Gly Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser  
                     180                      185                      190  
 Arg Glu Ile Leu Ser Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly  
                     195                      200                      205  
 Ala Cys Asn Ile Arg Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly  
 210                      215                      220  
 Val Arg Leu Gln Thr Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro  
 225                      230                      235                      240  
 Val Val His His Tyr Gly His Gly Ser Gly Gly Ile Ser Val His Trp  
                     245                      250                      255  
 Gly Thr Ala Leu Glu Ala Ala Arg Leu Val Ser Glu Cys Val His Ala  
                     260                      265                      270  
 Leu Arg Thr Pro Ile Pro Lys Ser Asn Leu

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 <222> 34  
 <223> polymorphic base C or T

<400> 13  
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<210> 24  
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<220>  
 <223> oligonucleotide 24-1457-52

<220>  
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 <223> polymorphic base C or A

<400> 24  
 tetgagatgc cctgtgtcc tetmagggag tagtggetga gcatttc 47

<210> 25  
 <211> 47  
 <212> DNA  
 <213> Artificial Sequence

<220>  
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<220>  
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<400> 25  
 cccagcctg ccactggcga gctytgtggc ctggggcaag ttacttc 47

<210> 26  
 <211> 47  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> oligonucleotide 24-1461-256

<220>

<231> allele

<232> 24

<233> polymorphic base A or G

<400> 26

gatggetctg gcattttcag ggarcagtea tgtctgatct caagttc

1

47